Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 24-27, 68-70, 77-80, 90-114 and 116-140 are pending in the application, with claims 70, 90, 98, 106, 114, 121 and 133 being the independent claims. Claim 115 is cancelled without prejudice to or disclaimer of the subject matter therein. Claims 114, 116 and 133 are amended. Support for the amendments to claims 114 and 116 can be found in original claim 115. Support for the amendment to claim 133 can be found on page 10, lines 1-15; pages 16-18 of the specification and in original claim 133. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 101

The Examiner has rejected claims 90-140 under 35 U.S.C. § 101. *See* Paper No. 14, pages 3-7. Specifically, the Examiner has alleged that "the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility." *Id.* at 3. In support of this rejection, the Examiner has asserted that "[t]he specification does not teach that the polynucleotide sequence of SEQ ID NO:3 is actually translated into protein which is expressed in any disease state." *Id.* at 3. The Examiner has also pointed out that "there is no evidence in the specification, or any art of record to indicate that galectin 9 [the expressed product of SEQ ID NO:3] would be capable of regulating apoptosis in a positive or negative

manner, or that the expression of galectin 9, or lack thereof, would be diagnostic for any disease state." *Id.* at 4. Finally, the Examiner has argued that despite the homology between galectin 9 and other, known galectins, there are "sequence dissimilarities" suggesting that "protein structure and function [of galectin 9] cannot be predicted." *Id.* at 5.

However, for the reasons given below, the Examiner has not made a *prima facie* case showing that galectin 9 (SEQ ID NO:4) lacks utility.

The Standard Used to Establish Utility Under 35 U.S.C. § 101

The USPTO has promulgated guidelines examiners must follow when applying rejections under 35 U.S.C. §101 in the context of amino acid sequences:

> When a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein.

See Utility Examination Guidelines, 66 Fed. Reg. 1092, 1096 (January 5, 2001). Persons skilled in the art find it reasonable to assign a new protein to a class of conserved proteins on the basis of sequence homology. Publications confirm the value of homology studies in predicting protein function and classifying new proteins. *E.g.,* Wilson *et al., J. Mol. Biol.* 297(1):233-49 (2000) (Exhibit A); des Jardins *et al.*, *ISMB* 5:92-99 (1997) (Exhibit B); Holm, L., *Curr. Opin. Struct. Biol.* 8(3):372-79 (1998) (Exhibit C). Thus, Applicants can assert that a particular claimed amino acid sequence is useful because that amino acid sequence is homologous with other known and useful proteins. Such an assertion must be accepted by the examiner unless a *prima facie* case is made to discount the homology. *Id.* at 1096.

Applicants Have Established Utility Under 35 U.S.C. § 101

Here, Applicants have ascribed a utility to a novel polypeptide based on its homology to an existing class of proteins which share a specific, substantial, and credible utility. In particular, the homology of SEQ ID NO:4 to other galectins is best observed in Figures 5A and 5B. These figures shows a sequence alignment of SEQ ID NO:4 with other galectin family members showing the conserved amino acid residues highlighted by black squares with white lettering.

Galectins function in modulating cell-cell and cell-matrix interactions. *See* specification, page 2, lines 12-19 and references cited therein. Galectin 1 and galectin 3 also affect an immune response and/or apoptosis. *See* specification, page 2, lines 20-29 and references cited therein. One of ordinary skill in the art would thus recognize that galectins are useful for purposes of detecting apoptotic disorders such as cancer or immunoregulatory disorders such as asthma. The skilled artisan could raise antibodies to detect galectins; their detection would be useful for diagnosing cancerous diseases or immunoregulatory diseases.

Applicants clearly set forth a diagnostic utility for galectin 9 (SEQ ID NO:4) based upon the known utility of other, useful galectins. Specifically, galectin 9 can be used to diagnose, *inter alia*, asthma and Hodgkin's disease. *See* specification, page 29, lines 3-9. These are respectively immunoregulatory and cancerous diseases. Thus, Applicants have asserted a substantial, specific and credible utility for galectin 9. This assertion is based upon galectin 9's (SEQ ID NO:4's) homology to other known and useful galectins.

The Examiner has not made a Prima Facie Case Showing Lack of Utility

The basis of the Examiner's 35 U.S.C. § 101 rejections of claims 90-140 is on three grounds:

i) the specification does not prove or provide evidence that SEQ ID NO:4 is actually expressed;

ii) the specification does not describe any clinical evidence or actual examples whereby a utility for SEQ ID NO:4 is demonstrated; and

iii) the sequence homology between SEQ ID NO:4 and other known galectins is not 100% and therefore its biological function cannot be determined.

Paper No. 14, pages 3-7. However, the Examiner has not met her burden of making a *prima facie* case showing lack of utility by making these arguments.

Evidence of Expression

The Examiner has alleged that utility for SEQ ID NO:4 is lacking because "[t]he specification does not teach that the polynucleotide sequence of SEQ ID NO:3 is actually translated into protein which is expressed in any disease state." Paper No. 14, page 3. Further, the Examiner has stated that "[e]ven if the expression of the polynucleotide of SEQ ID NO:3 did correlate with a disease state, one of skill in the art would . . . recognize that expression of mRNA does not dictate the translation of such mRNA into a polypeptide." *Id.* Finally, the Examiner cautions that "recent studies show that alternative splicing might affect more than 30% of human genes and the number of known post-translational modifications of gene products is increasing constantly so that complexity at protein level is enormous." *Id.*

at 6. However, these concerns do not negate the homology (discussed *supra*) which serves as a basis for Applicant's asserted utility for SEQ ID NO:4.

These rejections are clearly improper according to USPTO utility guidelines: "The suggestions to adopt a *per se* rule rejecting homology-based assertions of utility are not adopted." Utility Examination Guidelines, 66 Fed. Reg. 1092, 1096 (January 5, 2001). In contrast with the Examiner's rejection, the guidelines have provided an example of the sort of fact dependent scientific evidence that could be used to refute utility in sequence homology cases:

> For example, where a class of proteins is defined by common structural features, but evidence shows that the members of the class do not share a specific, substantial functional attribute or utility, despite having structural features in common, membership in the class may not impute a specific, substantial, and credible utility to a new member of the class.

Id. at 1096.

Here, the galectin class of proteins have a common structural feature as evinced by their homology. Moreover, galectins share a specific, substantial structural/functional attribute or utility in that they are implicated in cellular apoptosis and/or immunoregulation. *See supra*. In contrast with the guidelines, the Examiner has not put forward any evidence that refutes the facts in Applicants' instant specification which show that the galectin class of proteins have a specific, substantial and credible utility. Rather, the Examiner has only provided evidence of a *general* nature pertaining to the difficulty in assigning protein function from novel nucleotide sequences. A specific utility cannot be refuted by general evidence: "It is imperative that Office personnel use specificity in setting forth an initial rejection under 35 U.S.C. 101 and support any factual conclusions made in the *prima facie* showing." Manual of Patent Examining Procedure (M.P.E.P.), § 2107.01, subsection IV (emphasis in original).

Furthermore, Applicants wish to point out that SEQ ID NO:4 was derived from a cDNA library which is generated by collecting mRNA. The existence of such mRNA is strong evidence that SEQ ID NO:4 is expressed. Although the Examiner has correctly indicated that protein expression can be regulated at the translational level, she has not provided any evidence that transcribed SEQ ID NO:3 (i.e., mRNA encoding SEQ ID NO:4) is not translated into SEQ ID NO:4. By citing Alberts *et al.*, the Examiner has merely shown that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. This only suggests that ferritin mRNA is occasionally not translated. Alberts *et al.* does not suggest that ferritin mRNA is *never* translated. Indeed, it would be a wasteful expenditure of cellular energy to create mRNA which is *never* translated.

Clinical Evidence or Actual Examples Showing Utility are not Required

The Examiner has alleged that utility for SEQ ID NO:4 is lacking because "there is no evidence in the specification, or any art of record to indicate that galectin 9 (SEQ ID NO:4) would be capable of regulating apoptosis in a positive or negative manner, or that the expression of galectin 9, or lack thereof, would be diagnostic for any disease state." Paper No. 14, page 4. However, the M.P.E.P. indicates that a 35 U.S.C. § 101 rejection on these grounds should only rarely be made:

> Requests for additional evidence should be imposed rarely, and only if necessary to support the scientific credibility of the asserted utility (e.g., if the asserted utility is not consistent with the evidence of record and current scientific knowledge). As the Federal Circuit recently noted, '[o]nly after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.' *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995) (citing *In re Bundy*, 642 F.2d 430, 433, 209 USPQ 48, 51 (CCPA 1981)).

M.P.E.P. § 2107.01, subsection V. Here, the Examiner has provided no specific art of record that is inconsistent with Applicants' asserted utility for SEQ ID NO:4. Rather, Applicants have asserted utility of SEQ ID NO:4 based on its homology to other known galectins having specific and substantial utilities. As described above, such homology based utilities are credible. Until the Examiner provides specific, fact oriented scientific evidence that refutes Applicants' asserted utility, Applicants are not required to submit evidence.

100% Sequence Homology is Not Necessary to Support Homology Based Utility

The Examiner has raised the concern that "even if the disclosed hypothetical proteins share sequence homology with other galectins, they also exhibit sequence dissimilarities and the effects of these dissimilarities upon protein structure and function cannot be predicted." Paper No. 14, page 5. The Examiner has also cited several scientific publications which show *generally* that substituting a single amino acid residue in a protein sequence *can* destroy biological activity. *Id.* at 5-6.

But perfection or "statistical certainty" of the evidence presented in an application is not required for an assertion of utility to be valid. *See* M.P.E.P. § 2107.01 (VII.); *Nelson v. Bowler*, 626 F.2d 853, 856-57 (C.P.P.A. 1980). Nor is a "rigorous correlation" required between the evidence provided and the asserted utility. *Fujikawa v. Wattanasin,* 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). All that is required under 35 U.S.C. § 101 is that the assertion be "reasonably predictive" of the utility. *E.g., Rey-Bellet v. Englehardt,* 493 F.2d 1380 (C.P.P.A. 1974). Evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is credible or more likely than not true. M.P.E.P. § 2107.01 (VII.).

Contrary to the Examiner's contention, the state of the art shows that credible assertions of utility and function of a protein can be made based on homology studies. For example, *Wilson et al., J. Mol. Biol.* 297(1):233-49 (2000) (Exhibit A) indicates that "functional class is conserved for sequence identities as low as 20-25%." Figure 7A of Wilson *et al.* demonstrates that two proteins sharing as low as 20% sequence identity have a *greater than 70% chance* of being a member of the same functional class. Other publications further confirm the value of homology studies in predicting protein function. *E.g.*, des Jardins *et al.*, *ISMB* 5:92-99 (1997) (Exhibit B; "The most successful technique for identifying possible function of anonymous gene products . . . is performing similarity searches against sequence databases."); Holm, L., *Curr. Opin. Struct. Biol.* 8(3):372-79 (1998) (Exhibit C; "By inferring homology between two proteins on the basis of sequence similarity, biologists can confidently predict that protein structure and function have remained similar during evolution."). Thus, Applicants have presented results that show a high, and sufficient degree of homology that one would consider the utility to be credible. (*See* Figures 5A and 5B).

Exhibits

As discussed above, Applicants do not consider the Examiner's rejection to be proper. Assuming, *arguendo*, that the Examiner properly made the rejection, Applicants have provided post-filing date references which obviate the Examiner's utility rejection.

Applicants submit herewith Matsumoto, R. *et al., J. Biol. Chem. 273*:16976-16984 (1998); (Exhibit D). Matsumoto *et al.* disclose the ecalectin protein and nucleotide sequence. The ecalectin protein is identical to the galectin 9 protein of the invention, with only one exception: ecalectin has twelve consecutive amino acids (PPGVWPANPAPI) not found in

NOT THE SAME

galectin 9. (Note that ecalectin's fifth amino acid residue was later corrected to glycine. *See* Table II of Matsushita, N. *et al.*, *J. Biol. Chem. 275*:8355-8360(2000); Exhibit E.) Ecalectin is an eosinophil chemoattractant (ECA) produced by T-cells and expressed during allergic and parasitic responses. Exhibit D at 16976. As indicated by Matsumoto *et al.*, "(e)osinophil accumulation is a common feature of many inflammatory diseases such as bronchial asthma, allergic rhinitis, helminth infection, and atopic dermatitis." *Id.* at 16976. Thus, when an antigen stimulates a T-cell response, ecalectin is released by T-cells attracting eosinophils to a particular location. no mention of chemoattractant qualities in spec.

Applicants' instant specification recognizes that galectin 9 (SEQ ID NO:4) plays a role in immune response and asthma in particular. *E.g.*, specification page 27, lines 20-25. Galectin 9 is useful for purposes of raising antibodies which can be used to diagnose asthma in a human patient. *See* specification page 25, line 22 to page 27, line 18; in particular, *see* page 26, lines 12-15. Thus, Applicants have asserted a substantial, specific and credible utility for the galectin 9 protein. This assertion has been further supported by Exhibits D and E.

no mention

Applicants' galectin 9 is also useful for diagnosing or prognosing a patient for Hodgkin's disease. *See* specification, page 29, lines 5-9. Matsumoto *et al.* and Matsushita *et al.* also indicate that ecalectin is an allelic variation of a human gene described by Türeci *et al.*, also named galectin 9. *See* Exhibit D, pg. 16981; Exhibit E, pg. 8358; and Türeci *et al., J. Biol. Chem.* 272:6416-6422 (1997), (Exhibit F). Türeci *et al.*'s galectin-9 is an antigen selectively expressed by patients with Hodgkin's lymphoma. *See* Exhibit D, pg. 16983; Exhibit F, pg. 6421. Therefore, Türeci *et al.*'s galectin-9 is useful for diagnosing or prognosing a patient for Hodgkin's disease.

boundary list

only 50/0

The epitopic regions of Applicants' galectin 9 are included in the specification from page 11, line 21 to page 12, line 2. (Applicants' galectin 9 epitopic regions differ from the corresponding stretches of Türeci *et al.*'s galectin 9 *by only 3 amino acid residues*. Moreover, Applicants' epitopic regions are 100% identical to Matsumoto *et al.*'s ecalectin, which was demonstrated *supra* by Matsushita *et al.* to be the same as Türeci *et al.*'s galectin 9. Also note that none of ecalectin's additional twelve consecutive amino acids fall within the epitopic regions.) Furthermore, peptides at least six amino acid residues in length, when derived from a given protein, will consistently elicit antibodies that bind to the original protein. (*See* Harlow *et al.*, Antibodies A Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pp. 76 (1988); Exhibit G). Hence, the epitopic regions of Applicants' galectin 9 which are identical to the corresponding stretches of Türeci *et al.*'s galectin 9 are clearly long enough to be used to raise antibodies which can detect Türeci *et al.*'s galectin 9. *See also* specification, page 26, lines 16-19. Hence, Applicants' galectin 9 can be used to raise antibodies to diagnose or prognose Hodgkin's disease. *See* specification, page 29, line 3 to page 30, line 2. Thus, Applicants have asserted a substantial, specific and credible utility for galectin 9 (SEQ ID NO:4). This assertion has been further supported by Exhibits D, E, F and G.

Although the Examiner has indicated more than one basis from which the utility rejection is developed, Applicants respectfully point out that they only need to "provide one credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement." *See* Utility Examination Guidelines, 66 Fed. Reg. 1092, 1098 (January 5, 2001). Applicants note that galectin 9's (SEQ ID NO:4's) utility as described above is not

limiting. Rather, Applicants assert that galectin 9 has utility that extends beyond its use in diagnosing asthma or Hodgkin's disease.

Although Applicants have provided evidence in support of their assertion that galectin 9 (SEQ ID NO:4) is useful, Applicants respectfully argue that the Examiner has not met the burden of making a *prima facie* case showing that galectin 9 lacks utility. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the 35 U.S.C. § 101 rejections as they have been applied to claims 90-140.

Rejections under 35 U.S.C. § 112

35 U.S.C. § 101 as a Basis for 35 U.S.C. § 112 Rejections

The Examiner has rejected claims 1, 2, 13 and 25 under 35 U.S.C. §112, first paragraph as not supported by a well established utility for the reasons set forth in the 35 U.S.C. §101 rejections above, and therefore not enabling one skilled in the art to use the invention. Applicants respectfully point out to the Examiner that claims 1, 2, 13 and 25 were not elected in the Reply to the Second Restriction Requirement (filed November 20, 2000). Furthermore, the Examiner has indicated that only claims 90-140 are examined on the merits. Paper No. 14, page 2.

The Examiner has also used the 35 U.S.C. §101 utility rejection (*supra*) as the basis of a 35 U.S.C. §112 enablement rejections with respect to claims 90, 92, 94-98, 100, and 102-140. For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and credible utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107(IV) at 2100-28.

Therefore, since the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejection of claims under 35 U.S.C. § 112, first paragraph, based on lack of utility of the claimed invention, should be withdrawn. Applicants respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 112 as it applies to claims 90, 92, 94-98, 100, and 102-140.

Amino Acid Sequences at Least 95% Identical

The Examiner has also rejected claims 90, 92, 94-98, 100, 102-105, 128 and 129 under 35 U.S.C. §112 for lack of enablement. In particular, the Examiner contends that the specification is not enabling for claims drawn to proteins comprising amino acid sequences which are at least 95% identical to SEQ ID NO:4. The Examiner bases this rejection on the assertion that "it could not be predicted that a polypeptide that differs from SEQ ID NO:4 by as much as 5% would function as suggested." Paper No. 14, pg. 8. The Examiner has also provided evidence that single amino acid mutations can defeat biological function. In particular, the Examiner cites a reference by Burgess *et al.* to demonstrate that substitution of a single lysine residue in the protein acidic fibroblast growth factor led to the loss of heparin binding. Paper No. 14, page 8. The Examiner has also cited a reference by Lazar *et al.* to further demonstrate that replacement of an amino acid residue can result in a reduction of biological activity. *Id.*

Although the Examiner has provided two examples wherein changing a single amino acid residue results in a loss or reduction of biological protein function, these examples are not indicative of all deletions, additions or substitutions to amino acid sequences. The examples are also not relevant to galectin 9 which is an entirely different protein sequence, not

described or discussed by the Examiner's references. Moreover, Bowie *et al.* teaches that the "message [for encoding proteins] is highly degenerate in that many different sequences can code for proteins with essentially the same structure and activity"; and that "proteins are surprisingly tolerant of amino acid substitutions." *See* Bowie, J.U. *et al.*, *Science* 247:1206-1210 (1990). For example, it is well known in the art that the majority of amino acid substitutions within the beta subunit of hemoglobin are functionally "silent." *See* Hutt *et al.*, *Hemoglobin* 20(4):371-6 (1996)(Exhibit H; "Approximately 700 hemoglobin variants have been reported, causing a variety of clinical manifestations, with the majority being clinically silent.") These studies serve to demonstrate that proteins often retain activity notwithstanding changes in their amino acid sequence. Thus, contrary to the suggestion made by the Examiner, Applicants assert that, in general, proteins are resilient to modification and retain functional activity notwithstanding numerous amino acid substitutions, deletions and/or insertions. This assertion is found in the specification, for example, from page 21, line 7 to page 23, line 12.

Moreover, the references cited by the Examiner only describe the effect an amino acid substitution has on the indigenous biological function of the specified proteins. There is no discussion in the Examiner's cited references as to the effect the single amino acid substitution has on the functional ability of those specified proteins to raise specific antibodies. Peptides at least six amino acid residues in length, when derived from a given protein, will consistently elicit antibodies that bind to the original protein. (*See* Harlow *et al.*, Antibodies A Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pp. 76. (1988); Exhibit G.) Hence, amino acid sequences that differ by as much as 5% from SEQ ID NO:4 but retain the epitopic regions are capable of functioning in the antibody diagnostic method as disclosed in the

specification. Predicted epitopic regions are included in the specification from page 11, line 21 to page 12, line 2. A person of ordinary skill in the art in changing up to 5% of the residues in SEQ ID NO:4 would know not to make changes to the epitopic regions for purposes of raising antibodies. As discussed above, Applicants have explained that asthma can be diagnosed using antibody-based techniques targeting galectin 9. *See* specification page 29, line 3 to page 30, line 2. Hence, sequences which differ by up to 5% yet maintain an epitopic region are useful for purposes of raising antibodies which can be used to diagnose asthma in a human patient. *See* specification page 25, line 22 to page 27, line 18; in particular, *see* page 26, lines 12-28.

Therefore, the cited references fail to support the assertion that any and all amino acid changes in SEQ ID NO:4 would have a dramatic effect on all functional utilities. Moreover, because the epitopic regions of SEQ ID NO:4 have been described, a person of ordinary skill in the art is enabled to make changes in the amino acid sequence of up to 5%, without effecting those epitopic regions. *See* specification page 26, lines 12-28. Applicants respectfully request that the Examiner reconsider and withdraw this rejection under 35 U.S.C. § 112 as it applies to claims 90, 92, 94-98, 100, 102-105, 128 and 129.

Proteins Comprising Fragments of SEQ ID NO:4

The Examiner has also rejected claims 106-127 and 130-132 under 35 U.S.C. §112 for lack of enablement. In particular, the Examiner contends that the specification is not enabling for claims drawn to proteins comprising fragments of SEQ ID NO:4. The Examiner bases this rejection on the assertion that a fragment of SEQ ID NO:4 relocated in a different

protein sequence would not necessarily have the same three dimensional conformation as that found in SEQ ID NO:4.

Assuming, *arguendo*, that the Examiner is correct, Applicants note that antibodies against linear epitopes are useful, for example, in western blots. Here, three dimensional conformations are irrelevant for diagnostic or prognostic screening purposes, as described in the specification on page 26, lines 12-19. Further, the specification teaches at page 26, lines 20-28 amino acid residues which are predicted to be epitope-bearing portions of SEQ ID NO:4. With this information, for example, sufficient guidance is provided for identifying which fragments of SEQ ID NO:4 would be capable of raising antibodies to SEQ ID NO:4. One of ordinary skill in the art in designing an amino acid sequence including a fragment of SEQ ID NO:4 for raising antibodies would know to use these epitopic regions in order to produce a protein which is still useful for raising galectin 9-specific antibodies.

Thus, Applicants assert that the specification clearly teaches one of ordinary skill in the art which particular amino acid fragments can be utilized without further changing the function of the protein as related to generating antibodies. Applicants respectfully request the Examiner to reconsider and withdraw this rejection under 35 U.S.C. § 112 as it applies to claims 106-127 and 130-132.

Proteins Encoded by Polynucleotides Which Hybridize to the Protein Coding Region of SEQ ID NO:3 or the Complement Thereof

The Examiner has also rejected claims 133-140 under 35 U.S.C. §112 for lack of enablement. In particular, the Examiner contends that the specification is not enabling for claims drawn to proteins encoded by polynucleotides which hybridize to the protein coding region of SEQ ID NO:3 or the complement thereof. With respect to polynucleotides which

hybridize to the protein coding region of SEQ ID NO:3, claim 133 has been amended to obviate this rejection. In particular, claim 133 is no longer directed to a protein encoded by a polynucleotide which hybridizes to SEQ ID NO:3.

With respect to proteins encoded by polynucleotides which hybridize to the complement of the coding region of SEQ ID NO:3, the basis of the Examiner's rejection is that these claims "encompass a variety of polypeptide variants and it would be expected that a substantial number of the hybridizing or complementary polynucleotides encompassed by the claims would not encode protein which would share either the structural or asserted functional properties with . . . SEQ ID NO:4 . . . ." Paper No. 14, page 10.

As discussed *supra*, the specification discloses which stretches of SEQ ID NO:4 are antigenic and useful for purposes of raising antibodies (*see* page 26, lines 20-28). Thus, an altered version of SEQ ID NO:3 can be generated with multiple changes; yet, which maintains unaltered the corresponding nucleotide stretches which encode the epitopic regions. A person of ordinary skill in the art will recognize that if the epitope encoding regions are preserved, a wide range of nucleotide changes in SEQ ID NO:3 can still accommodate i) its hybridization to the complement of SEQ ID NO:3 and ii) a nucleotide sequence which encodes a polypeptide useful for raising galectin-9 specific antibodies. A person of ordinary skill in the art would also recognize that the genetic code is degenerate and that multiple silent mutations can be made without effecting either the epitopic or other regions of SEQ ID NO:4. Applicants respectfully request the Examiner to reconsider and withdraw this rejection under 35 U.S.C. § 112 as it applies to claims 133-140.

Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 114 and 119 under 35 U.S.C. § 102(b) as being anticipated by Massa *et al., J. Biol. Chem. 270*:5032-5038 (1995), as evidenced by Accession Number P47967. The results of a homology search of SEQ ID NO:4 has revealed that it and P47967 both share a stretch of 20 contiguous amino acids. Accordingly, claim 114 has been amended to obviate the rejection. Applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 102(b) as it applies to claims 114 and 119.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Aaron L.Schwartz
Agent for Applicants
Provisonal Registration No. P-48,181

Date: 6/15/01

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

Version with markings to show changes made

The title has been amended.

Claim 115 has been cancelled.

Claim 114 (once amended). An isolated protein comprising [15] 30 contiguous amino acids of SEQ ID NO:4.

Claim 116 (once amended). The protein of claim [115] 114 comprising 50 contiguous amino acids of SEQ ID NO:4.

Claim 133 (once amended). An isolated protein comprising amino acid residues encoded by a [first] polynucleotide which hybridizes to [a second polynucleotide having the nucleotide sequence] the polynucleotide complement of the coding region of SEQ ID NO:3[, or the complement thereof,] under the following conditions:

(a) incubating overnight at 42°C in a solution consisting of 50% formamide, 5x SSC, 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA; and

(b) washing at 65°C in a solution consisting of 0.1x SSC;

wherein said [first] polynucleotide encodes a protein having a biological activity selected from the group consisting of:

(a) lactose binding activity; and

(b) binding activity for an antibody having specificity for a polypeptide consisting of the complete amino acid sequence of SEQ ID NO:4.